Le Voyageur Temps

The truth about artificial sweeteners – Are they good for diabetics?

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ABSTRACT

Artificial sweeteners are thought to be beneficial for diabetics or obese where refined sugar can be a problem. These low-calorie sweeteners are seemingly safe to use, provide sweetness without calories, and provide a choice of sweet foods to those who otherwise cannot partake them (refined sugars). However, while artificial sweeteners may indeed restrict calories most of them have no beneficial effects on control of diabetes mellitus; rather possibly increase its risk. Additionally, there could be some other safety concerns possibly risk of cancer.

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1. Background

Artificial sweeteners a.k.a. non-nutrient sweeteners (NNS) came in vogue during the World War I & II when due to agricultural crisis sugar production was falling. During this time Saccharin was accepted very well as low cost alternative to sugar. Fahlberg accidentally discovered the sweet properties of saccharin which made his dinner bread very sweet when he forgot to wash hands after a long day in lab.[1] Since then several artificial sweeteners have been discovered and produced: Aspartame, Neotame & sucralose are a few of them. These substances can be found in more than 6000 food products across the globe. Some newer products such as sucralose and plant product stevia are more metabolically neutral.

2. Community use of artificial sweeteners

In recent past there has been a rising pandemic of obesity in all population and ethnic groups and due to aggressive marketing campaigns within food industry, role of these artificial sweeteners has evolved from sugar substitutes to health substitutes. Due to extreme sweetness of these products minimal amount is required to provide sweetening without added calories (of sugar). Thus these substances are being marketed to the masses as healthy alternative to sugar especially for diabetic population (e.g. sucralose as sugar free), and as an alternative to sugar sweetener in beverages such as Diet coke (main consumer being healthy young). Although these claims appear promising, they have never been confirmed in any vigorously conducted trial or large epidemiological study. On the other hand, only a well planned, prospective, epidemiological study, with a frequent and long duration follow up can answer these questions; health hazard & adverse effect, if any, of these substances. Another major limitation of studies evaluating the impact of these substances is,

unregulated use of these substances among masses in some developing countries, so that many food substances inadvertently have these agents already added on and it may become difficult to discriminate which processed day-to-day food stuffs have them and which do not. Indeed, Tripathi and co-workers, in a study conducted in Lucknow, revealed that even in children of age group 6-10 year, consumption of artificial sweeteners exceeded Accepted Daily Intake (ADI) by 54% (due to consumption of ice candies & crushed ice).[2] Habitual pan masala users also consume above average (above ADI) artificial sweeteners. Finally, overall poor health care infrastructure and reporting of disease related data in developing world, makes it a formidable task to find out long term impact of these unique compounds and elucidate development of various disease entities (as a result of usage of these compounds) despite several safety concerns about them which are raised from time to time.

3. Safety issues

Recent safety concerns about them came from a large epidemiological study as well as small physiological studies in human.[3,4] In a physiological studies of artificial sweetener both aspartame and sucralose were associated with significant postprandial hyperglycemia in comparison to Stevia. Postprandial insulin level was also high with artificial sweeteners suggesting that artificial sweetener may be associated with metabolic abnormalities.[5] Physiological evidence included consumption in the form of in diet soda/soft drinks. In a large meta-analysis of prospective studies (17 cohorts with 38 253 cases) it has been shown that artificial sweeteners were associated with risk of type 2 diabetes mellitus (T2DM), and may not be as healthy alternative to sugar sweetened beverages as projected. Even though publication bias cannot be ruled out for artificial sweeteners, a recently published E3N EPIC Cohort study was unique in that it collected 10

year data among more than 10 000 women among consumer of NNS as packet & tablets.[6] This study actually demonstrated an association between NNS usage and risk of diabetes. More importantly they were also able to show a gradation of risk depending upon year of consumption & amount consumed per day. Another explanation given for a probable association between artificial sweeteners and T2DM in observation studies is reverse causation bias because of increase intake of artificial sweeteners among obese.[7] However in this study even after excluding cases of incident T2DM during first 5 year of follow up there was a positive association between artificial sweeteners and T2DM suggestive of no significant reverse causation effect in the study. Strength of the study was that reverse causation was not found to be a confounder and risk of T2DM was independent of traditional diabetic risk factors. However in a large study, Dekoning and co-workers, who prospectively analyzed more than 40 000 participants, reported that in white men, sugar sweetened beverages were significantly associated with T2DM (OR 1.15 $P < .01$) although artificial sweeteners per se may not (OR 1.05 $P < .12$).[8] Nevertheless the possible risk of diabetes cannot be ignored as these substances are being marketed extensively as an alternative to sugar especially among diabetic population. In a double blind, randomized controlled trial 477 healthy school going children received sugar containing beverage with sucrose or beverage with artificial sweeteners containing sucralose & aspartame combination. At 18 month of follow-up artificial sweeteners were significantly associated with reduced weight gain as compared to sucrose.[9] They concluded that decreased sugar consumption may lead to decrease in insulin level and satiety, leading to less weight gain. Whether caloric restriction by decreasing sugar beverages and substituting it with artificial sweetener can lead to reduced obesity & T2DM is still controversial because of the possibility of compensatory appetite and increased overall food intake. Thus although artificial sweetener may be used as a method of dietary modification to reduce add on sugar

consumption; however weight gain and glycemic control is still linked to total energy consumption. Latest ACC/AHA guidelines also recommend a word of caution with the use of artificial sweetener as a means of calorie restriction.[10]

Another important safety concern with artificial sweeteners is the risk of carcinoma which was first demonstrated by various animal studies. Cyclamate was the first artificial sweetener to be banned due to risk of carcinoma. Weihrauch and colleagues reviewed the literature meticulously and opined that there was no significant evidence of artificial sweetener consumption and cancer risk with currently available artificial sweeteners.[11] Similar conclusions were also drawn by Lim and co-workers who prospectively analysed data from more than 400 000 men & women over a period of 5 years and did not find any association between aspartame consumption & risk of hematopoetic or brain tumours.[12] One prospective analysis has linked artificial sweetener aspartame consumption with risk of lymphoma & leukaemia only in men.[13] However, this study was limited by inability to quantify exact consumption of aspartame because of variable presence of aspartame among the dietary sources. Another limitation of this study was the inability to explain the rational behind male preponderance of carcinoma risk (Tables 1 and 2).

4. Difficulty in conducting prospective trials

Since their discovery more than hundred year ago artificial sweetener are now identified as a constituent of more than 6000 food products of mass consumption alone or in combination with other agents because of bitter after taste of some of them (e.g. saccharin). These factors make it very difficult to conduct a randomized controlled trial co-relating pattern of artificial sweetener consumption and various diseases. Thus, despite industry pitch, a host of outcome studies not showing favourable effect (if not downright harm) should be an important consider-

Table 1
Artificial sweeteners commercially available.

Sweeteners	×Sweeter than sugar	Metabolism	Brand name	Acceptable daily intake (ADI)	Possible side-effects
Saccharin	300	Nil, bitter metallic after taste	Sweet 'N low	5	Bladder cancer
Aspartame	200	Metabolized to: Phenylaanine Aspartic acid Methanol	Equal/ NutraSweet	50	Chronic fatigue, brain tumor
Acesulfame	200	Nil	Sweet one	15	Carcinogenic
Neotame	8000	By esterase	New tame	18	Neurotoxic, immunotoxic and excitotoxic
Sucralose	600	Nil	Splenda	5	Possible DNA damage, may affect insulin sensitivity
Stevia	150	Steviol glycosides are poorly absorbed in GI tract; small amounts absorbed are metabolized in liver	Truvia/ PureVia	4	–

*ADI (Acceptable Daily Intake: mg of sweetener/kg body weight/day) while EDI (The Estimated Daily Intake) is based on the amount consumed by people whose intake exceeds that of 90% of the population, in developed world this value is well below ADI).

Table 2
Artificial sweetners in common food products.

Common foodstuff	Constituent artificial sweeteners
Sugarless cookie	Acesulfame K & sucralose
Diet Coke/Coca Cola zero	Aspartame & acesulfame K
Coca Cola Life	Cane sugar + stevia
Diet Pepsi	Aspartame/sucralose
Chocolate syrup	Acesulfame K & sucralose
Sugarfree traditional Indian sweet (Halwa/Khoya Barfi/Rasgolla)	Aspartame & acesulfame K & sucralose
Chewing gum	Aspartame & acesulfame K
Pan masala	Saccharin
Sweet supari	Cyclamate-saccharin mixture
Ice candies and crushed ice	Saccharin

ation limiting their use. On the other hand, despite these general assumptions, substances like sucralose and Stevia which do not get metabolized in the body seems to be safe as minimal/no intestinal absorption take place.

5. Conclusions

Artificial sweeteners have been in vogue for a long time and are now constituents of many processed foods. They have been in use for control of obesity and diabetes mellitus. While they may reduce the caloric intake, per se they may not have any beneficial effects on control of diabetes because they may themselves alter the insulin sensitivity. In addition they may have other safety concerns like cancer.

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